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10/532,264	12/28/2005	Yasuko Nakagawa	082368-004000US	4474

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EXAMINER	
KOLKER, DANIEL E	

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1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/532,264	NAKAGAWA ET AL.	
	Examiner	Art Unit	
	DANIEL KOLKER	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-32,34,35 and 41-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-32,34,35 and 41-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks and amendments filed 11 September 2008 have been entered. Claims 29 – 32, 34 – 35, and 41 - 44 are pending and under examination.

Withdrawn Rejections and Objection

2. The following rejections and objections set forth in the previous office action are withdrawn:

A. Any rejection of a claim now canceled is moot.

B. The rejection under 35 USC 112, second paragraph, drawn to the indefinite nature of the phrase "stringent conditions" (paragraph 9 on p. 6 of the office action mailed 30 June 2008) is withdrawn in light of the amendments.

C. The rejection of claim 32 under 35 USC 112, second paragraph (paragraph 10 on p. 6 of the office action mailed 30 June 2008) is withdrawn in light of the amendments which clarify the scope of the claim.

D. The rejection under 35 USC 102(e) over Jensen is withdrawn in light of the amendments to the claims. The claims no longer encompass methods of using antibodies that bind to proteins with infinite possible divergence from disclosed sequences.

E. The rejection under 35 USC 102(e) over Buck is withdrawn in light of the amendments to the claims. The claims no longer encompass methods of using antibodies that bind to proteins with infinite possible divergence from disclosed sequences.

Maintained Rejections

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29 – 32, 34 – 35 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of selecting cells comprising contacting the cells with antibodies that bind to proteins with the sequence of SEQ ID NO:3 or 4 or variants at least 80% identical to same, does not reasonably provide enablement for methods comprising contacting cells with proteins encoded by any and all nucleic acids which hybridize under the

conditions recited in claims 29 and 32 part (v). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection is maintained for the reasons previously made of record. Briefly, element (v) of claims 29 and 32 allows for methods of using an antibody which binds to a protein, wherein the protein is encoded by a nucleic acid that hybridizes to the complement of SEQ ID NO:1 or 2 under certain recited conditions. The encoded protein is required to have certain structural elements including a transmembrane domain and Ig domains, but there is no degree of sequence identity required for the protein to which the antibody binds. The nucleic acids that hybridize to the complements of SEQ ID NO:1 or 2 include those with frame-shifting mutations, i.e. those nucleic acids that have deletions of one or two nucleic acids, thereby encoding proteins entirely different from those of either SEQ ID NO:3 or 4. The encoded protein need have no degree of structural identity with any disclosed sequence. As set forth in the previous office action, the skilled artisan would have to determine, on his or her own, how to use antibodies that bind to sequences other than SEQ ID NO:3 or 4. Given the lack of guidance in the specification, the large degree of experimentation that a skilled artisan would have to undertake would clearly be undue.

Applicant did not traverse the examiner's determination that an unduly large degree of experimentation would be required, but rather stated that the claims have been amended so that they no longer read on methods of using antibodies that bind to very different proteins. The examiner disagrees, as explained above. The claims encompass methods of using antibodies that bind to variants of SEQ ID NO:3 or 4 with little if any structural similarity. Therefore this rejection is maintained. This rejection might be overcome by deleting element (v) of claims 29 and 32, or alternatively by amending element (v) to recite some degree of sequence identity to a disclosed protein sequence.

4. Claims 29 – 32 and 34 – 35 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

This rejection is maintained for the reasons previously made of record and explained in further detail below. Briefly, claims 29 and 32, part (v) of each claim, encompasses methods of using antibodies that bind to proteins encoded by nucleic acids which hybridize with the complement of SEQ ID NO:1 or 2. This includes using antibodies that bind to proteins encoded by frameshift mutations in the nucleic acids, as there is no requirement for any degree of identity at the amino acid level. The specification does not disclose the sequences of the frameshift mutations, and does not disclose the physical structure (e.g., amino acid sequence) of the antibodies that bind to them. Additionally, the specification fails to disclose methods of using antibodies that bind to these structurally different proteins. As the specification fails to describe to the public either the proteins encoded by the variant nucleic acids or the antibodies that bind them, independent claims 29 and 32 fail to meet the written description requirement of 35 USC 112, first paragraph. Claims 30 – 31 and 34 – 35 stand rejected as they depend from these independent claims but are not limited to embodiments which are completely described by the specification.

Rejections and Objections Necessitated by Amendment

Claim Objections

5. Claim 32 is objected to because of the following informalities: it recites "a cell population comprising dopaminergic precursor cell", which should read "a cell population comprising dopaminergic precursor cells". Note the phrase "dopaminergic precursor cell" appears multiple times within the claim; applicant should ensure that all instances are corrected as needed. Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 43 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Part (iii) of each of claims 43 and 44 is indefinite because it is drawn to a method of using an antibody that binds to a protein, wherein the protein is lacking "a signal sequence portion". While signal sequences of proteins are generally known to be located at the N-

terminus, the claim is confusing because it does not indicate how much of the protein can be deleted, and does not either explicitly specify what constitutes the signal sequence or "a signal sequence portion" of the protein. Since the claim is drawn to a method of using an antibody that binds to such a protein, given that the skilled artisan could not determine how much of the protein is to be deleted, the artisan could not determine if any given antibody that binds to a portion of SEQ ID NO:3 or 4 is within or beyond the scope of the claim.

Additionally, part (ii) of each of claims 43 and 44 is confusing because they recite “SEQ ID NO:4 or 4”; the use of “or" implies that the two sequences are different. However, SEQ ID NO:4 is of course identical to itself. The claim is confusing because it is unclear how a single sequence can both be identical to itself and distinct from itself.

New Rejections

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 29, 31 – 32, 35, and 41 – 44 are rejected under 35 U.S.C. 102(b) as being anticipated by Carulli (WO 01/98630, published 27 December 2001, cited as reference AB on IDS filed 10 February 2006).

This rejection is maintained for the reasons of record with respect to claim 32, and expanded to claims 29 and 41 – 44 as explained below. Carulli teaches a 708 amino-acid protein referred to as either gp354 or SEQ ID NO:8; the protein and encoding nucleic acid are set forth in Figure 7 from the reference. As indicated by the sequence alignment, the prior art protein is 85.6% identical to applicant’s SEQ ID NO:3 and differs from that sequence by 40 conservative substitutions, 66 mismatches, 5 deletions, and two gaps. Note that the alignment shows there are many regions of 100% identity between Carulli’s protein and instant SEQ ID NO:3, including but not limited to residues 31 – 47, 64 – 75, 118 – 137, 243 – 279, and 586 – 622 (using applicant’s numbering scheme, note this is the line labeled “Qy” on the alignment

included with the previous office action). Carulli also teaches antibodies to this protein; see p. 63 line 23 – p. 73 line 19, particularly p. 64 lines 8 – 11. Given the many identical epitopes between Carulli's SEQ ID NO:8 and applicant's SEQ ID NO:3, the antibodies from Carulli will inherently bind to SEQ ID NO:3, even though the two proteins are not 100% identical.

Carulli teaches the step of contacting the antibodies with samples comprising cells; see p. 89 final paragraph and p. 90 first paragraph. This is relevant to claims 29 and 32, each of which require contacting antibodies with cells. Carulli also teaches comparing the amount of the sample bound by the antibody to a control sample (p. 90 fist paragraph). This is the same as the "selecting" step recited in claim 29 and the "obtaining" step recited in claim 32. Since the step of comparing the amount of cells bound by the antibody requires "selecting" and "obtaining", each of which is a very broad term, the claims are anticipated. Note the claims do not require isolation of the cells that have bound to the antibodies, or culturing of such cells. Were such language included in the claims, this rejection might be overcome. However applicant is reminded not to introduce new matter into the claims in violation of 35 USC 112, first paragraph.

The examiner has included claims 41 – 44 in this rejection as well. As stated above, even though the two proteins (that from Carulli and present SEQ ID NO:3) are not identical, given the many regions of identity between the proteins, the antibodies taught by Carulli will necessarily bind to SEQ ID NO:3. Additionally, claims 31 and 35 are anticipated. Carulli indicates residues 22 – 510 of SEQ ID NO:8 are the extracellular domain (p. 45 lines 28 – 30), and given the many regions of identity between the two proteins within this region, the antibodies from Carulli will bind to an extracellular region of SEQ ID NO:3.

8. Claims 29, 31 – 32, 35, and 41 – 44 are rejected under 35 U.S.C. 102(a) as being anticipated by Sun (2003) Genomics 82(2):130-142. Note the cover page of the reference indicates it was available online 11 June 2003.

Sun teaches a protein called Kirrel2. As evidenced by the sequence alignment mailed with the previous office action, the protein is 99.7% identical to applicant's SEQ ID NO:3. Sun also teaches antibodies to this protein; see p. 132 final paragraph – p. 134 second column line 5. Given the very high sequence homology between Sun's protein and that of applicant's SEQ ID NO:3, the antibodies will bind to SEQ ID NO:3; this is on point to claims 29, 31, and 41 – 44. Additionally, the antibodies will bind to an extracellular domain, since the proteins are virtually

identical in their extracellular regions; this is on point to claims 31 and 35. Note that Sun teaches immunohistochemical staining of tissue from heart, brain and other tissues (p. 133 first complete paragraph). This includes the steps contacting the samples, which comprise cells, with the antibody, followed by staining with the chromogen DAB (see p. 141 first column, section entitled Immunohistochemistry). This staining is a form of selecting as recited in claim 29; those cells which have the Kirrel2 protein are selectively stained, those which do not have the label are not stained. Thus the reference anticipates claim 29 and dependent claims 31, 41, and 43. The staining also results in "obtaining" a cell population, and therefore the reference anticipates claims 32, 35, 42, and 44. Note the independent claims do not require isolation of the cells that have bound to the antibodies, or culturing of such cells. Were such language included in the claims, this rejection might be overcome. However applicant is reminded not to introduce new matter into the claims in violation of 35 USC 112, first paragraph.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 29 – 32, 34 – 35, and 41 – 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carulli (WO 01/98360) in view of Jensen (U.S. Patent Application Publication 2004/0241170, of record).

The reasons why claims 29, 31 – 32, 35, and 41 – 44 are anticipated by Carulli are set forth in the rejection under 35 USC 102(b) above. Briefly, the reference teaches contacting samples comprising cells, including neural tissue, with antibodies which will necessarily bind to SEQ ID NO:3, given the large number of identical epitopes, and teaches "selecting" and "obtaining" cells. While Carulli teaches determining the amount of gp354 in the samples, and suggests that such samples should be contacted with antibodies that bind to same, and teaches the artisan of ordinary skill how to make these antibodies (see for example p. 63 line 23 – p. 73 line 19), the reference does not explicitly teach flow cytometry as recited in claims 30 and 34.

Jensen teaches methods of using antibodies to purify cells that are neural in phenotype. For example, at paragraph [0061] – [0067] Jensen teaches using cell sorting techniques to purify antibody-bound cells from a heterogeneous population, which include the step of selecting antibody-bound cells. Jensen indicates that the antibody can be labeled (paragraph [0062]), which would allow for quantification of the cells. The methods of Jensen are known as flow cytometry, which is encompassed by claims 29 and 32 and recited in claims 30 and 34. However Jensen does not teach methods of using antibodies within the scope of independent claims 29 and 32.

It would have been obvious to one of ordinary skill in the art to modify the method of Carulli, who teaches identifying test cells and determining the amount of gp354 protein, by performing the steps set forth in Jensen, thereby arriving at the invention of claims 30 and 34. It would be reasonable to expect success, since Jensen teaches that one can label the antibody to allow for quantification, as does Carulli (see p. 71 line 4 - p. 72 line 17).

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANIEL KOLKER whose telephone number is (571)272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel E. Kolker/
Primary Examiner, Art Unit 1649
November 25, 2008